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(21) International Application Number: PCT/IT98/00069 (22) International Filing Date: 27 March 1998 (27.03.98) (30) Priority Data: RM97A000185 1 April 1997 (01.04.97) IT (71) Applicant (for all designated States except US): SIGMA-TAU INDUSTRIE FARMACEUTICHE RIUNITE S.P.A. [IT/IT]; Viale Shakespeare, 47, I-00144 Rome (IT). (72) Inventor; and (75) Inventor/Applicant (for US only): CAVAZZA, Claudio [IT/IT]; Piazza Campitelli, 2, I-00186 Rome (IT). (74) Common Representative: SIGMA-TAU INDUSTRIE FAR- MACEUTICHE RIUNITE S.P.A.; Viale Shakespeare, 47, I-00144 Rome (IT).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: NUTRITIONAL SUPPLEMENT FOR FACILITATING SKELETAL MUSCLE ADAPTATION TO STRENUOUS EXERCISE AND COUNTERACTING DEFATIGATION IN ASTHENIC INDIVIDUALS (57) Abstract <p>A nutritional supplement for facilitating the adaptation of skeletal muscle in individuals undergoing programs of strenuous exercise and counteracting defatigation and weariness in asthenic individuals is disclosed, which comprises a combination of L-carnitine, acetyl L-carnitine and propionyl L-carnitine as basic active ingredients. Optional ingredients comprise isovaleryl L-carnitine, branched-chain aminoacids and creatine and/or phosphocreatine.</p>		

Preferably, the essential amino acid mixture consists of the branched-chain amino acids valine, leucine and isoleucine.

The nutritional supplement of the invention may advantageously also comprise non-essential amino acids, particularly glutamine, L-glutamic acid, L-aspartic acid and L-asparagine.

An example of the nutritional supplement of the invention comprises:

- 10 (i) from 40 to 60% by weight of a mixture of L-carnitine, acetyl L-carnitine, propionyl L-carnitine, or their pharmacologically acceptable salts;
- (ii) from 10 to 15% by weight of valine;
from 10 to 15% by weight of leucine;
15 from 10 to 15% by weight of isoleucine; and
- (iii) from 8 to 12% by weight of creatine or phosphocreatine.

If non-essential amino acids are present, the nutritional supplement will also comprise from 10 to 30% by weight of such amino acids.

20 To all the effects and purposes of the present invention, what is meant by L-carnitine, acetyl L-carnitine, propionyl L-

CLAIMS

1. A nutritional supplement which comprises a combination of:
 - (a) L-carnitine;
 - (b) acetyl L-carnitine;
 - (c) propionyl L-carnitine;or the pharmacologically acceptable salts thereof, and a pharmacologically acceptable excipient thereof.
2. The nutritional supplement of claim 1, wherein the weight ratio (a):(b):(c) ranges from 1:1:1 to 1:0.1:0.1.
3. The nutritional supplement of claim 2 which further comprises :
 - (d) isovaleryl L-carnitine or a pharmacologically acceptable salt thereof,wherein the weight ratio (a):(b):(c):(d) ranges from 1:1:1:1 to 1:0.1:0.1:0.1.
4. The nutritional supplement of any of the preceding claims which further comprises an essential aminoacid or mixtures thereof.
5. The nutritional supplement of claim 4 wherein the essential aminoacid is selected from the group of the branched-chain aminoacids valine, leucine and isoleucine or mixtures thereof.

6. The nutritional supplement of claim 4, wherein the weight ratio between the combination of L-carnitine, acetyl L-carnitine, propionyl L-carnitine and the essential aminoacid or the mixture thereof ranges from 3:1 to 1:1.
7. The nutritional supplement of claims 4-6 which further comprises glutamine, L-glutamic acid, L-aspartic acid and L-asparagine.
8. The nutritional supplement of any of the preceding claims which further comprises a creatine selected from creatine and phosphocreatine.
9. The nutritional supplement of any of the preceding claims which comprises:
 - (i) from 40 to 60% by weight of a mixture of L-carnitine, acetyl L-carnitine and propionyl L-carnitine or the pharmacologically acceptable salts thereof;
 - (ii) from 10 to 15% by weight of valine;
from 10 to 15% by weight of leucine;
from 10 to 15% by weight of isoleucine; and
 - (iii) from 8 to 12% by weight of creatine or phosphocreatine.
10. The nutritional supplement of claim 9, which further comprises from 10 to 30% by weight of non-essential aminoacids.